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09/778,187	02/06/2001	Peter Robert Baum	2873-US	9057

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EXAMINER
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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/778,187	Applicant(s) BAUM ET AL.	
	Examiner Jessica H. Roark	Art Unit 1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 May 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18-63* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18-63* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☐ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *19* .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other:

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's Response, filed 5/27/03 (Paper No. 17), is acknowledged.
Claims 1-17 have been canceled previously.
Claims 18-63 are pending and under consideration.

2. No action was required of Applicant regarding the previous comment at paragraph #3. The Examiner simply wished to note that the amino acid sequences were the same.

3. The text of those sections of Title 35 USC not included in this Action can be found in a prior Action.
This Office Action will be in response to applicant's arguments, filed 5/27/03 (Paper No. 17).
The rejections of record can be found in the previous Office Action (Paper No. 15).

It is noted that a New Ground of Rejection is set forth herein. Accordingly, this Office Action is Non-Final.

Claim Rejections - 35 USC § 112 second paragraph

4. Claims 18-63 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 18-63 are indefinite in that they only describe the "LDCAM polypeptide" and "B7-L1 polypeptide" to which the claimed polypeptide binds by arbitrary protein names. There is nothing in the claims which establishes the metes and bounds of which polypeptides can be considered a "LDCAM polypeptide" or "B7-L1 polypeptide". Consequently, the metes and bounds of the polypeptide which binds are not established.

Applicant argues in the response filed 5/27/03 that these phrases are adequately described in the instant specification as filed. However, the description pointed to in the specification is not a definition which clearly establishes the identity of the polypeptides bound, but instead the specification states that the term encompasses a genus of related polypeptides. Therefore, the metes and bounds are not established.

It is again suggested that Applicant amend the claims to include a recitation of a SEQ ID NO(s) for each of the "LDCAM" and "B7-L1" polypeptides to either of which the instantly claimed polypeptides must bind.

B) Claims 35, 36 and 46-54 are ambiguous in reciting hybridizing under conditions of "moderate stringency" (claims 35 and 46-54) or "severe stringency" (claim 36). There does not appear to be a definition in the specification as filed that clearly provides the metes and bounds of these conditions. Thus it is unclear which conditions are actually claimed.

Applicant argues in the Response filed 5/27/03 that the paragraph bridging pages 9 and 10 sets forth these conditions. However, the bridging paragraph of pages 9-10 does not define these conditions, but rather only indicates certain parameters that are "included".

C) Applicant is reminded that any amendment must point to a basis in the specification so as not to add new matter. See MPEP 714.02 and 2163.06.

Claim Rejections - 35 USC § 112 first paragraph

5. Claims 18-63 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

SEQ ID NOS:2 and 4 (encoded by the DNAs of SEQ ID NOS:1 and 3); internal fragments of SEQ ID NO:2 or 4; polypeptides *comprising* fragments of SEQ ID NO:2 or 4 wherein the fragment is the extracellular domain of SEQ ID NO:2 or 4 and the polypeptide binds the "LDCAM" polypeptide of SEQ ID NOS:2 or 4 or binds the "B7-L1" polypeptide of SEQ ID NOS:8 or 10; and polypeptides *of limited sequence variation* that bind the "LDCAM" polypeptide of SEQ ID NOS: 2 or 4 or bind the "B7-L1" polypeptide of SEQ ID NOS: 8 or 10;

does not reasonably provide enablement for polypeptides that

a) comprise a sequence that has "at least 80% (or 90%) identical" (e.g., claims 18-21);
b) binds to any "LDCAM" or "B7-L1" polypeptide (all pending claims);
c) *comprises* fragments other than the extracellular domain (e.g., claims 22-34); or
d) comprise an amino acid sequence "variance" of unlimited number of insertions, deletions, or substitution (e.g., claims 55-63).

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The rejection of record may be found in full in Paper No. 15 and is incorporated herein as if set forth in full.

Applicant argues in the Response filed 5/27/03 that although some experimentation may be required to produce the variant polypeptides recited in the instant claims, the experimentation is not "undue". Applicant points to sections of the specification generally describing how to make variant polypeptides, and how to screen these variants for binding to LDCAM or B7L-1 polypeptides. Applicant argues that the references supporting unpredictability in the art previously provided by the Examiner are not relevant because in the instant case the polypeptide has a known function of binding to both other LDCAM polypeptides or to a B7L-1 polypeptide.

However, the examiner maintains that the experimentation is undue because the specification does not appear to provide sufficient guidance as to which residues should or should not be changed to preserve the recited function of binding either a LDCAM or B7L-1 polypeptide. Although the specification does provide working examples of human and mouse LDCAM polypeptides of SEQ ID NOS:2 and 4, the variation permitted by the instant claim language is extensive.

Metzler et al. (Nature Structural Biol. 1997; 4:527-531, of record) is particularly relevant to the unpredictability associated with introduction of changes to the amino acid sequence and the corresponding effect on the ability of the polypeptide to interact with a particular ligand because Metzler et al. show that any of a variety of single amino acid changes can alter or abolish the ability of CTLA4 to interact with its ligands CD80 and CD86 (e.g., summarized in Table 2).

Statements in the specification to go forth and make mutant sequences without guidance as to where the changes should be introduced does not provide the skilled artisan with sufficient guidance.

The absence of a defined structure for the LDCAM or B7L-1 polypeptide to which these variants bind further increases the unpredictability associated with making variants that bind.

Regarding the insufficient guidance provided as to the scope of polypeptides encompassed by the terms "LDCAM" and "B7L-1", Applicant argues that the specification describes the genus of molecules encompassed by these terms, therefore, adequate guidance has been provided.

However, in the absence of sufficient structural information (e.g., amino acid sequence, etc.), there is insufficient guidance and direction to allow the skilled artisan to determine whether any particular polypeptide is either a "LDCAM" or "B7-L1" polypeptide without the need for further undue experimentation

Consequently, the experimentation required to make variants which bind any "LDCAM" or "B7L-1" polypeptides is unnecessarily, and improperly, extensive and undue.

It is again suggested that Applicant limit the claims to variant nucleic acids sequences having only limited variation (e.g. 95% identity) over the full length of the sequence, AND possessing testable functional activity supported in the specification and priority documents (e.g., binding a *particular* "LDCAM" or "B7-L1" polypeptide, as provided by inclusion of a SEQ ID NO:).

It is again noted that the instant claims recite in various forms polypeptides comprising "fragments" of a certain number of amino acid residues of the various SEQ ID NOS (or encoding nucleic acids). "Comprising" language opens the claim up to the inclusion of additional residues of undisclosed identity and number flanking the recited "fragment". The skilled artisan can make fragments *limited* to *sub*sequences of the individual SEQ ID NOS without undue experimentation. However, before the skilled artisan can make polypeptides comprising "fragments" with additional flanking sequence, guidance is required with respect to the identity of those flanking sequences. In the instant case however, the specification does not appear to provided this needed guidance. Therefore the scope of the instant claims encompassing "fragments comprising" does not appear to be commensurate with the enablement provided by the instant disclosure.

In addition, it is unpredictable if a fragment other than a fragment that is the extracellular domain would have the instantly recited function of binding a LDCAM or B7-L1 polypeptide (even were the LDCAM and B7-L1 polypeptides defined by SEQ ID NOS). The specification does not appear to provide guidance as to which fragments other than the fragments comprising the extracellular domain would have this activity. Therefore the scope of the instant claims does not appear to be commensurate with the enablement provided by the instant disclosure.

Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. For the reasons set forth supra, the experimentation left to those skilled in the art with respect to the instantly recited limitations is unnecessarily, and improperly, extensive and undue.

Claim Rejections – 35 U.S.C. § 102

6. The Declaration filed on 5/27/03 under 37 CFR 1.131 has been considered but is ineffective to overcome the Baker et al. (US 2002/0198147) reference of record.

The Baker et al. reference is a U.S. patent application publication of a pending or patented application that claims the rejected invention. An affidavit or declaration is inappropriate under 37 CFR 1.131(a) when the reference is claiming the same patentable invention, see MPEP § 2306. If the reference and this application are not commonly owned, the reference can only be overcome by establishing priority of invention through interference proceedings. See MPEP Chapter 2300 for information on initiating interference proceedings. If the reference and this application are commonly owned, the patent may be disqualified as prior art by an affidavit or declaration under 37 CFR 1.130. See MPEP § 718.

The rejection of record providing New Grounds of rejection based upon the claimed subject matter is set forth below.

7. Claims 18-63 are rejected under 35 U.S.C. 102(e) as being anticipated by Baker et al. (US 2002/0198147, of record), as evidenced by the alignments of record in Paper No. 15.

Baker et al. teach *and claim* the isolated PRO355 polypeptide set forth in SEQ ID NO:61 (e.g., claim 12).

The PRO355 polypeptide is 100% identical to the instant polypeptide of SEQ ID NO:2 from position 39 to position 442. PRO355 differs from the instant polypeptide of SEQ ID NO:2 only by an internal deletion of two amino acid residues in the signal sequence corresponding to positions 24 and 25 of instant SEQ ID NO:2.

PRO355 therefore also is a polypeptide 100% identical to the instant polypeptide of SEQ ID NO:4 from position 8 to position 423. PRO355 differs from the instant polypeptide of SEQ ID NO:4 by an internal deletion of two amino acids in the signal sequence corresponding to positions 6 and 7 of instant SEQ ID NO:2 and by an additional amino acid at the C terminus.

Baker et al. also teach *and claim* the nucleic acid of SEQ ID NO:60 which encodes the PRO355 polypeptide of SEQ ID NO:61 (e.g., claim 1). The nucleic acid of SEQ ID NO:60 would hybridize to the complement of SEQ ID NO:1, including from 16 or 130 to 1137; and would hybridize to the complement of SEQ ID NO:3, including from 1 or 62 to 1069, under moderate or severe stringency in view of the sequence identity between the nucleic acid of SEQ ID NO:60 of Baker et al. and the instant SEQ ID NOS:1 and 3 encoding SEQ ID NOS:2 and 4.

Baker et al. also teach *and claim* methods of producing the PRO355 polypeptide by culturing a host cell transfected with the nucleic acid of SEQ ID NO:60 (see e.g., paragraph 297 and claim 11).

Baker et al. also teach *and claim* fusion polypeptides comprising the PRO355 polypeptide or a soluble extracellular domain (i.e., a fragment) thereof, including a fusion polypeptide comprising an Fc region (e.g., paragraphs 293-295 and claims 15-17).

Variants of the PRO355 polypeptide are also taught *and claimed* by Baker et al. (see e.g., paragraphs 180-187 and claims 12-13).

Compositions comprising the PRO355 polypeptide, fragments and variants thereof are taught at paragraphs 350-352.

The PRO355 polypeptide of Baker et al. inherently shares the functional properties of the instant polypeptides, including binding to a LDCAM polypeptide or a B7-L1 polypeptide. In addition, the PRO355 polypeptide would inherently form oligomers, including dimers, trimers or tetramers.

Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of the PRO355 polypeptide of Baker et al.

The reference teachings thus anticipate the instant claimed invention.

Conclusion

8. No claim is allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jessica Roark, whose telephone number is (703) 605-1209. The examiner can normally be reached Monday to Friday from 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

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July 31, 2003

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